REMARKS/ARGUMENTS

Claims 1, 2 and 5-45 are presently pending in this application. Claims 1, 2, 8-31, and 33-34 are amended herein. Claim 31 is amended and now provides the proper antecedent basis for the terms X1 and X2. Support for this amendment can be found in the specification and in claim 2. Claims 1, 2, 8-31 and 33-34 have been amended to correct minor errors, including the proper use of the connectors "and" and "or," the use of "is" instead of "may," and the addition of the phrase "in need of treatment". Support for these amendments can be found in the specification and claims as filed. No new matter has been added by these amendments.

Applicants request the addition of new claims 39 – 45. Support for these claims can be found in claims 32 – 38. No new matter has been added by these claims.

35 U.S.C. §112 First Paragraph

The Examiner has rejected claims 1 and 31-38 under 35 USC § 112 first paragraph stating that the specification, while being enabling for a linking group represented by the Formula IV, does not reasonably provide enablement for any linking group for the reasons set forth in the Office Action of August 10, 2004. The Examiner states that the specification fails to provide a specific definition for the linking group, and that the definition in claims 1 and 31-38 is not limited to the group of Formula IV. The Examiner maintains that the specification fails to provide any guidance or teaching on how to choose linking groups which do not have Formula IV, and further that the term "linking group" encompasses a large number of possible groups and that it would take undue experimentation to determine which specific linking groups will result in a compound having the desired activity.

This rejection is respectfully traversed. Claim 31 only is amended herein and is now directed only to compounds having a linking group of Formula IV. With respect to claim 1 and the claims dependent on it, Applicants submit that one of ordinary skill in the art is able to practice the full scope of the claimed invention described by these claims. See *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). "That is not to say that the specification itself must necessarily describe

how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003).

The use of linkers (or "spacers") to link two parts of a conjugate was well known at the time the priority application was filed, in July 2002. Therefore, unlike nascent technology, enablement for linker technology does not have to be included within the specification because a person of ordinary skill in the art is familiar with linkers and will have knowledge of linkers independent from the patentee's instruction. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004).

Evidence that linkers are well known and understood in the art can be found by looking at similar U.S. patents. In a survey of patents using either the term "linker" or "spacer" in the claims, we retrieved 416 patents having composition, compound, delivery, or agent in the title.[1] Of the first 15 patents related to the chemical arts retrieved, 9 defined the spacer or linker used and 6 did not.[2] Therefore, 40% of the patents (including the 20 issued most recently from applications prior to July 2002, and therefore subject to the current examination standards of the PTO) did not particularly define the linker or spacer in the broadest linker claim nor provide disclosure or enablement of all possible linkers in the specification. The relevant broad claims or claim sections of these patents are duplicated and presented collectively in Exhibit A. For example, U.S. Pat. 6,790,827 contains claim 24 directed to a method where the bioactive agent of claim 1 "is covalently bound indirectly to the cobalt atom of the organocobalt complex via a spacer." U.S. Pat.

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[1] Search performed at the USPTO Web site: (((ACLM/"a linker" OR ACLM/"a spacer") AND (((TTL/composition OR TTL/compound) OR TTL/deliver$) OR TTL/agent)) AND APD/19800101->20020701): Hits: 416 patents.

[2] The 6 patents are:
6,821,632 Composite of a vulcanizable rubber composition and cured rubber product
6,790,827 Bioconjugates and delivery of bioactive agents
6,787,517 Agent and methods for treating pain
6,783,819 Crown compound modified silica coatings for ink-jet media
6,777,237 Bioconjugates and delivery of bioactive agents
6,776,976 Bioconjugates and delivery of bioactive agents

6,787,517 claims an agent "wherein the therapeutic component and the targeting ligand are attached to each other through a spacer component" in claim 31.

Since the use of a broadly defined linker or spacer group was well-understood at the time this application was filed (as it was for these earlier-filed patents listed in footnote 2), the specification does not have to detail every possibility of the claimed linker to be enabling. Applicants therefore respectfully request reconsideration and withdrawal of this rejection. Nor do applicants ascribe to the activity or any other beneficial property of the claimed conjugates to the linker used to connect the two moieties. Thus, all a person of ordinary skill would have to do is device a linker that would react with and connect the macrolide moiety and the other NSAID moiety. It is submitted that this can readily be done in multiple ways with the exercise of a modicum of ordinary skill.

35 U.S.C. §112 Second Paragraph

The Examiner has rejected claims 1-2 and 5-38 under 35 USC 112, second paragraph, as being indefinite for failure to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asserts that the terminology "and pharmaceutically acceptable salts and solvates thereof and individual diastereoisomers thereof" in claims 1, 2 and 8-31 is an improper Markush terminology, and advises that the terminology "or a pharmaceutically acceptable solvate thereof on an individual diastereoisomer thereof" can be used to overcome the rejection. Claims 1, 2 and 8-30 have been amended and recite a proper alternative limitation. Claim 31 was not amended based on this rejection as this claim already recited a proper alternative language. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner states that the terminology "Rx may be" in claim 2 renders the claim indefinite because it fails to limit the definition of Rx to the groups set forth. Applicants have amended claim 2 to recite "Rx is." Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner maintains that there is no antecedent basis in the structural formula set forth in claim 31 for the variables X1 and X2 in the reaction steps. Claim 31 has been amended to recite proper antecedent basis and particularly describes the linker elements in the claim. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner asserts that in claims 33 and 34 it is unclear if the diseases set forth are treated at the same time or separately. Claims 33 and 34 have been amended to include the alternative "or" and clearly recite the method of treating alternative conditions or diseases. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Examiner states that the terminology "administering to a subject" in claim 33 makes it unclear whether said subject is in need of treatment. Claim 33 has been amended to include the phrase "in need of treatment" to more accurately identify the subject. Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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